REMARKS

I. Preliminary Remarks

In a telephone conversation with Examiner Ketter, the Applicant's representative informed the Examiner that new claims 45 and 46 were filed on 2 August 2004 prior to the mailing of the present office action and that the claims were not examined. As per the telephone conversation and as set out below, the Applicants submit that the rejections are not properly extendible to claims 45, 46 or 47.

Applicants respectfully request entry of claims 45 and 46 as filed on 2 August 2004 and the present amendments to those claims and new claim 47 in that they put the application in better form for allowance or appeal.

The claims are fully supported by the specification as filed.

In the event that the Examiner chooses not to enter Claims 45, 46, the amendments thereto and new claim 47, the following arguments are presented as to the patentability of the claims as currently pending. Arguments as to the patentability of the claims as amended are also presented herewith.

II. Patentability Arguments

A. The Cited Art Fails to Describe Every Element of the Claimed Invention and Cannot Anticipate the Present Claims and Therefore the Rejections Under 35 USC § 102(b) are Erroneous and Should Be Withdrawn.

Claims 32-39 and 43 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Tramontano (U.S. Patent No. 4,659,567, "Tramontano"). The rejection should be withdrawn because the reference fails to teach every limitation of the present claims. The applicants respectfully submit that the Examiner is ignoring explicit limitations of the instant claims. When the instant claims are properly viewed in their entirety, including all of the recited limitations, the applicants submit that the claims are novel over the art referred to by the Examiner because the art does not teach each and every element of the present claim as is required under the law to properly anticipate an invention.

It is well settled law that in order to anticipate a claim a prior art reference must disclose, either expressly or inherently, all of the limitations of the claims. *Transclear Corp. v. Bridgewood Services*, 290 F.3d 1364, 62 USPQ2d 1865 (Fed.Cir. 2002). See also *Gechter v. Davidson*, 116 F.3d 1454, 1456, 43 USPQ2d 1030, 1032 (Fed.Cir. 1997). ("Under 35 U.S.C. § 102, every limitation of a claim must identically appear in a single prior art reference for it to anticipate the claims"); *United States Filter Corp. v. Ionics, Inc.*, 68 F.Supp.2d 48, 55 USPQ2d 1071, 1077 (D.Mass. 1999), ("If a prior art reference lacks any claimed element, then as a matter of law, a decision maker (whether in the Patent Office or in a Court) cannot find any anticipation.") Indeed, this principal of law is in accordance with the findings of many courts that in order to infringe a product-by- process claim, the alleged infringer must practice the claimed process and that a similar or the same product made by a different process does not infringe a product-by-process claim. See, *e.g., Atlantic Thermoplastics Co., Inc. v. Faytex Corp.*, 970 F.2d 834, 846 (Fed. Cir. 1992) ("Thus, process terms in product-by-process claims serve as limitations in determining infringement.") A common principal uniting these series of cases is that all of the elements of a claim must be considered under both the anticipation and infringement analysis. Yet in the present case, the Examiner continues to studiously ignore explicit claim elements in finding that the present claims are anticipated by the Tramontano reference which fails to teach the process elements of the present claim.

The Examiner has characterized the instant claims as being "drawn to antibodies, more narrowly recited as catalytic antibodies, made by the recited process." The Examiner has characterized Tramontano as teaching "antibodies which catalyze chemical reactions." However, Tramontano teaches the production of antibodies raised in an animal and by hybridoma technology. The present invention is concerned with antibodies and in particular catalytic antibodies produced by a synthetic method in which a genetic library is generated and represents the immune repertoire of an animal from which the antibody encoding sequences are obtained and which are used to express and select desired antibodies. More specifically, the present invention provides a catalytic antibody by a method in which a large number of different antibody variable region genes (i.e., V_L and V_H) is cloned and expressed in expression vectors. The inventors described and used a set of DNA primers which are capable of hybridizing to a much larger number of antibody genes allowing amplification of these genes using PCR which results in a genetically diverse population of V_H or V_L coding sequences.

More specifically, the applicants respectfully submit that the presently claimed combination of features is novel, distinct and defines a product, specifically, an antibody and more particularly a catalytic antibody or antibody fragment produced by the recited method and selected for its ability to bind a particular ligand/antigen substrates and catalyzes an enzymatic reaction.

Among the claim elements not taught by Tramontano are:

(a) synthesizing a V_H-coding gene library containing a plurality of different V_H-coding DNA sequences by a method comprising the steps:

(i) preparing a polynucleotide containing composition, wherein at least a portion of the polynucleotides in said composition comprise a plurality of difference V_H-coding sequences,

(ii) amplifying a plurality of V_H-coding sequences in said polynucleotide containing composition;

(b) synthesizing a V_L-coding gene library containing a plurality of different V_L-coding DNA sequences by a method comprising the steps:

(i) preparing a polynucleotide containing composition, wherein at least a portion of the polynucleotides in said composition comprise a plurality of different V_L-coding sequences,

(ii) amplifying ~~a~~ said plurality of V_L-coding sequences in said polynucleotide containing composition;

(c) joining in operable combination V_H-coding sequences from said V_H-coding gene library with V_L-coding sequences from said V_L-coding gene library into expression vectors as to be able to coexpress a V_H-coding sequence and a V_L-coding sequences from each vector, whereby a diverse library is formed;

(d) selecting and isolating from said diverse library at least one coexpression vector capable of producing polypeptides having the desired specificity;

(e) transforming a host cell with said expression vector; and

(f) isolating an antibody encoded by said vector from said host cell.

(See canceled claim 32.)

The antibody thus selected may be a catalytic antibody (see canceled claim 33).

Because Tramontano fails to disclose all of claimed elements of the present invention, the applicants respectfully submit that the rejection of claims 32-39 and 43 under 35 U.S.C. § 102(b) is improper should be reconsidered and withdrawn and further that the rejections are not properly extendible to currently amended claims 45 and 46 and newly presented claim 47.

Claims 45, 46, As Amended, and New Claim 47

Claims 45, 46 (as amended) and new claim 47 are now directed to methods of making an antibody to an antigen. The Applicants respectfully submit that the rejections based on Tramontano are not properly extendible to claims 45 and 46 as originally filed, and as now amended. As amended, the claims are directed to methods for making and antibody to an antigen the method comprising the indicated steps. Tramontano does not teach any of the recited claim elements but rather is directed to making an antibody in an animal. Because Tramontano does not teach the presently claimed method, the Applicants submit that it cannot anticipate the present claims and therefore the rejections under 35 U.S.C. § 102(b) are not properly extendible to claims 45, 46, and 47.

B. The Rejections of Claims 32-39 and 43 Based On An Alleged Lack of Sufficient Written Description Under 35 USC §112, First Paragraph is Erroneous and Should Be Withdrawn

Despite the detailed description of the structure, sequence function of the catalytic antibodies and antibody fragments encompassed by the present claims provided by the specification, the Examiner has improperly rejected claims 32-39 and 43 as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to a person of ordinary skill in the art, at the time the invention was filed, that the inventor had possession of the claimed invention. More precisely, the Examiner improperly requires the applicants to provide precise structures of members of the genus of catalytic antibodies or antibodies fragments. The Applicants respectfully submit that the law does not require the elucidation of precise structures of species within a genus and to do so now is improper.

The purpose of 35 USC § 112, first paragraph, is to ensure that the inventor had possession, as of the filing date of the application relied on of the subject matter claimed. In *Re Alton,* 76 F.3d 1168, 1172, 37 USPQ2d 1578, 1581 (Fed. Cir. 1996). How the specification accomplishes this is not material. *Id.* The written description requirement is satisfied if a skilled artisan would have understood the inventor to be in possession of the claimed invention. "Although [the applicant] does not have to describe exactly the subject matter claimed, the description must clearly allow persons of ordinary skill in the art that [he or she] inventors invented what is claimed". *In re Gosteli,* 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed.

Cir. 1989) (citation omitted). "[T]he test for sufficiency of support in patent application is whether the disclosure of the application relied upon reasonably conveys to the artisan that the inventor had possession of the later claimed subject matter". *Id,* citing *Ralston Purina Co. v. Far-Mar-Co. Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1989), quoting, *In re Kaslow* 707 F.2d 1366, 1375, 217 USPQ 1059, 1096 (Fed. Cir. 1983).

Written description may be satisfied through disclosure of relevant identifying characteristics, *i.e.*, structure, other physical and/or chemical characteristics, functional characteristics when correlated with a known or disclosed correlation between function and structure or some combination of such characteristics. See, Guidelines for Examination of Patents Applications Under 35 USC § 112, ¶1, *Written Description Requirement*, 66 Fed. Reg. 1099, 1106.

Other examples of relevant identifying characteristics include a sequence, a structure, binding affinity, binding specificity, molecular weight and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics can demonstrate the requisite possession. For example, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. *See Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997) ('written description' requirement may be satisfied by using 'such descriptive means as words, structures, figures, diagrams, formulas, etc. that fully set for the claimed invention').

The present specification provides abundant description of the claimed subject matter in terms of structural and functional characteristics and by way of example to illustrate substrates for the catalytic antibodies of the present invention and thus meets the written description requirement of 35 U.S.C. § 112, first paragraph. More particularly, the present invention is directed to catalytic antibodies or antibody fragments produced by the recited methods. The structure of immunoglobulin (antibody) molecules and parts thereof are described *inter alia* in the specification by the molecule types "IgD, IgG, IgA, IgM and IgE." *(Specification, page 15, line 35, - page 16, line 1)*. Their structures are further described as comprising "... two heavy (H) and light (L) chains with both a variable (V) and constant (C) region present on each chain." *(Specification, page 16, lines 1-4)*. Further, the applicants submit that the structure and function

of such molecules are well known by persons of ordinary skill in the art as being capable of binding to a wide variety of ligands such as antigens or enzyme substrates. The specification also describes additional structural features of the molecules stating that,

> "[S]everal different regions of an immunoglobulin contain conserved sequences useful for isolating an immunoglobulin repertoire. Extensive amino acid and nucleic acid sequence data displaying exemplary conserved sequences is compiled for immunoglobulin molecules by Kabat et al., in Sequences of Proteins of Immunological Interest, National Institutes of Health, Bethesda MD 1987.
>
> "The C region of the H chain defines the particular immunoglobulin type. Therefore the selection of conserved sequences as defined herein from the C region of the H chain results in the preparation of a repertoire of immunoglobulin genes having members of the immunoglobulin type of the selected C region."
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> "The V region of the H or L chain typically comprises four framework (FR) regions each containing relatively lower degrees of variability that includes lengths of conserved sequences. The use of conserved sequences from the FR1 and FR4 (J region) framework regions of the V_H chain is a preferred exemplary embodiment and is described herein in the Examples. Framework regions are typically conserved across several or all immunoglobulin types and thus conserved sequences contained therein are particularly suited for preparing repertoires having several immunoglobulin types."
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> *Specification, page 16, lines 4-31.*

The specification also delineates examples of the size ranges of the V_H and V_L polypeptide chains stating that:

> "The individual V_H and V_L polypeptides will generally have fewer than 125 amino acid residues, more usually fewer than about 120 amino acid residues, while normally having greater than 60 amino acid residues, usually greater than about 95 amino acid residues, more usually greater than about 100 amino acid residues. Preferably, the V_H will be from about 110 to about 125 amino acid residues in length while V_L will be from about 95 to about 115 amino acid residues in length.
>
> The amino acid residue sequences will vary widely, depending upon the particular idiotype involved. Usually, there will be at least two cysteines separated by from about 60 to 75 amino acid residues and joined by a disulfide bond."
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> *Specification at page 21, line 26, through page 22, line 5.*

The specification also describes examples of association constants characteristic of the catalytic antibodies of the present invention (also referred to in the specification as receptors) according to the present invention stating:

> "the subject catalytic receptors have an association constant for the preselected substrates generally greater than 10^5M^{-1} or 10^6M^{-1} and preferably greater than 10^7M^{-1}.

Specification at page 28, lines 10-18.

Examples of sequences which constitute part of and are used in producing catalytic antibodies or antibody fragments according to the present invention are illustrated in Table 1, Table 2, Table 3, and Table 4 and in Figures 3 and 5.

Further, the Applicants have demonstrated that the claimed process produces antibodies that bind a transition state hapsten (NPN). (See, *e.g.,* Figure 13, described in detail at page 10, lines 9-18, and Example 18, particularly 18C and pages 84-85 of the specification which were subsequently shown to have predicted catalytic activity.)

Because the specification describes the catalytic antibodies or antibody fragment of the present invention by *inter alia* how they are made, by certain structural features, by the sequence of certain parts of the catalytic antibodies and by association constants, the applicants submit that the specification fully satisfies the written description requirement of 35 USC § 112, first paragraph and, therefore, the rejection of claims 32-39 and 43 should be withdrawn and that the rejection is not properly extendable to claims 45 and 46.

The Applicants also respectfully submit that the specification provides sufficient written description within its four corners by way *inter alia* of specific structural information, conserved sequences useful in preparing catalytic antibodies and which ultimately make up certain regions of the catalytic antibodies produced by the process of the present invention according to the present invention therefore the rejections under 35 USC § 112, first paragraph, are erroneous and should be withdrawn.

Claims 45 and 46, as amended, and new claim 47

The Applicants respectfully submit that the rejections under 35 U.S.C. § 112, first paragraph, are not properly extendible to claims 45 and 46, as amended, and new claim 47

because these claims are not directed to antibodies *per se* but rather are directed to methods for making antibodies by the clearly elucidated steps set out in the claims. The specification provides working examples of the claimed method provides abundant description of the methods of the invention.

Conclusion

In view of the above amendments and remarks, Applicant respectfully submits that the instant application is in condition for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

HOWREY SIMON ARNOLD & WHITE, LLP

By: 
David W. Clough, Ph.D.
Registration No.: 36,107

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HOWREY SIMON ARNOLD & WHITE, LLP
321 N. Clark Street, Suite 3400
Chicago, IL 6010
(312) 595-1408 (Telephone)
(312) 595-2250 (Fax)